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COMMUNICATION

Sterically hindered malonamide monomers for the step growth synthesis of polyesters and polyamides

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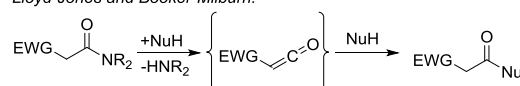
A new amide monomer for step growth polymerisation is reported: the chemistry exploits a bulky malonamide for the synthesis of polyesters and polyamides. No additives are needed and the only by-product, an amine, can be recycled.

With global polymer production increasing, new monomers for polymer synthesis will help to meet the associated challenges. In particular, polyesters and polyamides are vital components in packaging and textiles and are becoming increasingly important in state-of-the-art applications including biomedical materials and electronic technologies. There is particular interest in polyesters due to their universality: they are commodity chemicals with diverse applications ranging from insulation materials to LCDs and dielectric devices. They have a host of physical and chemical properties: can be thermoset, thermoplastics and curable resins whilst some are biodegradable and bio-renewable.¹ Global polyester production is set to increase from 28 million tonnes in 2005 to 40 million tonnes in 2015² and despite the prevalence of elegant ring-opening polymerisations being investigated in academia,³ industrial methods continue to rely on step growth polymerisation:^{4,5} the chemistry is well-developed and used on an industrial scale for the highly efficient synthesis of commodity plastics such as polyethylene terephthalate (PET) and polybutylene succinate (PBS). There is also tremendous scope in terms of polymer structure due to the range of inexpensive monomers that are readily available. Beyond the simple polycondensation of a carboxylic acid and nucleophile, alternative methods for step growth syntheses require the neutralisation and sequestration of HCl⁶ or the use of Lewis acids.⁷ Clearly, the development of new monomers will help to augment the step growth method of synthesis. For example, lower temperature pre-polymerisations would open up the potential to form new polymer compositions. New systems could also allow novel post-polymerisation modification pathways and mild, facile end group modification.

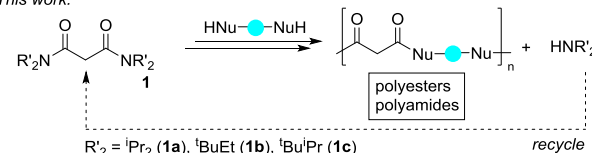
Herein, such a novel procedure is reported; the first use of a malonamide for the synthesis of polyesters. Inspired by a recent report from Lloyd-Jones and Booker-Milburn,⁸ the intriguing possibility of utilising sterically hindered malonamide

derivatives as monomeric building blocks was raised (Scheme 1).⁹ Taking advantage of the highly acidic α -CH₂, **1** is primed to undergo double nucleophilic addition¹⁰ through sequential ketene formation,^{11,12} allowing the growth of the polymer chain under comparatively mild conditions. Relief of strain through expulsion of the bulky amine will not only drive the polymerisation process but also allow recycling of the amine, increasing the overall atom-economy of the reaction. Through judicious selection of the dinucleophile, a library of novel polymers will be rapidly generated through this unique polymerisation pathway.

Lloyd-Jones and Booker-Milburn:



This work:



Scheme 1. Seminal results from Lloyd-Jones and Booker-Milburn show bulky amides undergo facile solvolysis. Described herein is the unprecedented use of a diamide to synthesise polymers.

As expected, sterics play a key role in reactivity: no reaction is observed when *N*-tetra(isopropyl)-malonamide (**1a**) is reacted with ethylene glycol. Increasing the steric bulk to the *N*-*tert*-butylethylamide analogue (**1b**) gives pre-polyester ($M_n = 1000 \text{ g mol}^{-1}$, PDI = 1.12, 18 h, 110 °C). Pleasingly, addition of a stoichiometric amount¹³ of ethylene glycol to **1c** (110 °C, 1 h) results in rapid formation of the desired pre-polyester ($M_n = 1900 \text{ g mol}^{-1}$, PDI = 1.37) with complete consumption of the starting monomer observed by ¹H NMR. Extending the reaction time to 18 h increases M_n ($M_n = 2100 \text{ g mol}^{-1}$, PDI = 1.52)¹⁴ whereas the use of a high b.p. solvent diminishes M_n .¹⁴ MALDI-TOF analysis reveals that the end groups (EGs) are *N*-*tert*-butylisopropylamide or alcohol. From EG analysis few cyclic species are observed and there is no evidence for

hydrolysis (except on quenching the pre-polymer).¹⁴ Likewise, NMR and MALDI-TOF analysis show no evidence for ketene dimerisation or Knoevenagel condensation⁶; the latter is likely to be assisted by the experimental conditions whereby the expelled *N*-*tert*-butylisopropylamine is collected immediately by distillation. This amine is isolated in high yield (> 95%) and purity (> 99%) and can be re-used to synthesise **1c**. This reaction is initiator-free (no metal catalysts are required) and the only by-product is the aforementioned amine.

A selection of diols has been explored in the synthesis of pre-polymers (Table 1). Again, complete loss of **1c** occurs in all cases and the transformation tolerates both long chain aliphatic and secondary diols with only a slight reduction in M_n (Entries 5 to 8). Spectroscopic analysis of these unsymmetrical systems (Entries 7 and 8), as expected, shows no preference for coordination of the R- or S-enantiomer. Spectroscopic investigation gives little evidence for discrimination between primary (1°) and secondary (2°) alcohol reactivity *i.e.* head-to-head [(2°-1°)-malonate-(1°-2°)] or head-to-tail [(2°-1°)-malonate-(2°-1°)] coordination along the polymer chain. The greater number of 2°-OH EGs is as expected since the 1°-OH is anticipated to react preferentially¹⁵ with the growing polymer chain. Aromatic systems are also tolerated, with *m*-benzenedimethanol polymerising with modest M_n (Entry 9). Phenolic substrates (hydroquinone, resorcinol and catechol) do not afford polymalonates: complete loss of the methylene signal is observed by ¹H NMR spectroscopy along with formation of several new aromatic signals. The low pKa of the phenolic monomers may result in adverse reactivity with the acidic methylene protons of **1c**.¹⁶

Table 1. Substrate scope for pre-polymer synthesis

Entry	Nucleophile	M_n (gmol ⁻¹) ^a	PDI ^a	T_g (°C) ^b
1	ethylene glycol	2100	1.52	-30.1, -19.6
2	1,3-propanediol	3000	1.53	-36.2
3	1,4-butanediol	2200	1.38	-47.5
4 ^c	1,8-octanediol	2200	1.66	not obs.
5 ^{d,e}	1,3-cyclohexanediol	1300	1.57	+28.4
6	(±)-1,2-butanediol	1500	1.44	-10.7
7	(±)-1,3-butanediol	1400	1.58	-33.7, -21.7
8 ^c	2,3-butanediol	1600	1.55	-4.2
9 ^c	<i>m</i> -benzenedimethanol	1100	1.47	-34.4, -19.4
10 ^{c,e}	ethylene diamine	500	1.08	not obs.
11 ^{c,e}	1,4-butanediamine	900	1.11	-62.6, +76.6
12 ^{c,e}	piperazine	900	1.11	+121.3
13 ^c	<i>p</i> -xylenediamine	700	1.12	+146.8
14 ^{d,e}	1,2-cyclohexanediamine	1100	1.18	+60.2

Conditions: **1c** (0.67 mmol), dinucleophile (0.67 mmol), 110 °C, 18 h.

^aDetermined by GPC. ^bDetermined by DSC. ^cOther transition points observed *i.e.* T_c , T_m , oxidation. ^d*cis* and *trans*. ^eDetermined by MALDI-TOF.

A range of T_g values are observed for these pre-polyesters. With the exception of 1,8-octanediol (Entry 4), all show a T_g but no melting or crystallisation temperature over the range analysed. The more sterically congested diols tend to give pre-polymers with a higher T_g (Entries 5, 6, 8).

Polyamides are also readily formed when **1c** is exposed diamines (Entries 10 to 14). Although pre-polyamide M_n is low these are the first reported examples of polytransamidation, indeed they are among only a handful of examples of catalyst-free transamidation reactions.⁸ Reaction of ethylenediamine in solution (Entry 10) is necessary to inhibit evaporation of the nucleophile: dilute conditions and loss of reagent is reflected in the lower M_n . DSC analysis appears more complex showing several transition points,¹⁴ including high T_g (Entries 11 to 14) T_c and T_m (Entries 10 to 12).

The pre-polymers are readily converted into high M_n polymer through subsequent condensation under vacuum (Table 2). As expected with step-growth polymerisations, broadening of PDI occurs as M_n increases. Ethylene glycol and 1,3-cyclohexanediol (Entries 1 and 5) appear to give very high M_n glass-like polymer, but only the low M_n washings are soluble in THF to allow for GPC analysis. DSC analysis shows small variations in the transition points,¹⁴ for example the polymer containing 1,3-propanediol repeat unit, T_g increased from -36.2 °C in the pre-polymer to -29.3 °C in the high M_n polymer (Table 2, Entry 2), whilst the ethylene glycol analogue now displays a crystallisation peak at 284.8 °C. Extended results, including vacuum condensation to form high M_n polyamides and full analysis of physical properties will be reported in due course.

Table 2. Conversion of pre-polymer into high M_n step-growth polymer is readily achieved.

Entry	Nucleophile	M_n (gmol ⁻¹) ^a	PDI ^a	DP
1 ^b	ethylene glycol	7,830	1.28	60
2	1,3-propanediol	20,260	1.74	141
3	1,4-butanediol	33,290	2.29	211
4	1,8-octanediol	24,770	2.27	116
5 ^b	1,3-cyclohexanediol	2,100	1.93	11
6	(±)-1,2-butanediol	15,320	1.90	97
7	(±)-1,3-butanediol	16,830	1.93	107
8	2,3-butanediol	15,670	3.62	99
9	<i>m</i> -benzenedimethanol	14,260	3.85	69

Conditions: pre-polymer (from Table 1), 60 °C, 0.05 mbar, 48 h. ^aDetermined by GPC. ^bLow molecular weight washings: bulk sample insoluble in THF.

Although the polyesters obtained have high M_n and are very competitive with leading examples of aliphatic step growth polymerisations,⁷ an attempt to further increase M_n was undertaken through the addition of various Lewis acids (LAs). Earlier reports from Yamamoto,^{7a} Takasu^{7b,d} and Kricheldorf^{7c} show how LAs can improve the M_n of step growth polyesters. It was pleasing to observe that addition of 20 mol% Cu(OTf)₂ results in a progressive increase of pre-polymer M_n with PDI remaining constant (M_n = 3300 gmol⁻¹, PDI = 1.40). With a stoichiometric amount of Cu(OTf)₂ no polymer product is observed by GPC,¹⁴ however copper-free polymer is observed by MALDI-TOF along with evidence for Cu-containing polymer, presumably coordinated through the carbonyl-oxygen atoms in a stable six-membered chelate.¹⁷

Reactivity in the presence and absence of Cu(OTf)₂ was compared through reaction monitoring of the pre-polymerisation process (Figure 1).

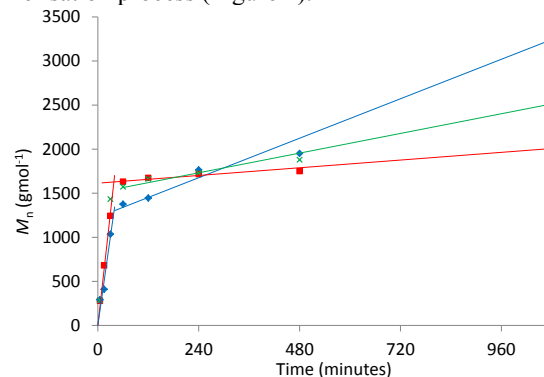


Figure 1. Monitoring M_n vs. time. ■ Cu-free 0–60 min: $y = 42.5x$, $R^2 = 0.985$; 60–1080 min: $y = 0.365x + 1614$, $R^2 = 0.977$. ♦ 20 mol% Cu(OTf)₂ 0–60 min: $y = 33.6x$, $R^2 = 0.924$; 60–1080 min: $y = 1.866x + 1228$, $R^2 = 0.983$. × 10 mol% Cu(OTf)₂ 0–60 min: $y = 48.0x$, $R^2 = 0.997$; 60–1080 min: $y = 0.930x + 1509$, $R^2 = 0.986$.

During the initial stages there is little difference between the Cu-free and Cu-mediated reactions. However, beyond this rapid induction period there is a concomitant levelling off in ΔM_n s: the Cu(OTf)₂ mediated reactions show a greater ΔM_n s until the point of quenching. ΔM_n s is doubled when the Cu(OTf)₂ loading is doubled (comparing 10 mol%, ✕, and 20 mol%, ◆, reactions from 60 min to 18 h).

Table 3 shows the effect of Cu(OTf)₂ on pre-polymerisation with alternative diols. It is evident that use of this particular LA has a positive impact on pre-polymer M_n but also causes an increase in PDI. Condensation of the pre-polymers under vacuum conditions gives plastics which, presumably due to the high M_n and presence of chelated Cu, are completely insoluble but flexible materials. A detailed study on the interactions of Cu(OTf)₂ with **1c**, its effect on polymerisation and physical analysis of these high M_n polymers is currently underway.

Table 3. Cu(OTf)₂ as an additive in polymerisation.

Entry	Nucleophile	M_n (gmol ⁻¹) ^a	PDI ^a
1	1,8-octanediol	2570	1.75
2	(±)-1,3-butanediol	1860	1.83
3	(±)-1,2-butanediol	1690	1.70
4	2,3-butanediol	2060	1.85
5	<i>m</i> -benzenedimethanol	1640	2.17

Conditions: **1c** (0.67 mmol), dinucleophile (0.67 mmol), Cu(OTf)₂ (0.134 mmol), 110 °C, 18 h. ^aDetermined by GPC.

In summary, a new monomer for step growth polymerisation has been developed: amides have been utilised for the first time in the synthesis of polyesters and polyamides. Many of the polymers have never been reported in the literature before.¹⁸ Atom economy is good, with easy recycling and reuse of the bulky amine whilst application of vacuum to the pre-polymer results in high molecular weight step growth polymers. Additives are unnecessary for polymerisation to occur, however, with careful selection of LA an increase in M_n is possible. It is envisaged that further exploration of alternative diamides will give access to a range of highly tuneable monomers with more controlled reactivity.¹⁹ Although the chemistry appears limited to monomers with an EWG adjacent to an α -CH₂, the synthesis of *N*-tert-butylisopropylsuccindiamide could furnish a new monomer for the synthesis of PBS.²⁰ In addition, metal coordination through the 1,3-dicarbonyl moiety could lead to a new range of metal-chelate monomers whilst the use of highly EW functional groups, including ferrocenyl units²¹, could also provide new motifs for metallopolymer synthesis.

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